Ocular manifestations of a metastatic adenocarcinoma in a horse

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Ocular Manifestations of a Metastatic Adenocarcinoma in a Horse

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ABSTRACT

A 10-year-old German Warmblood gelding was referred to the Equine Department of the Vetsuisse Faculty, University of Zurich, Switzerland for an iris mass OD, lethargy, intermittent fever, and coughing. Ophthalmic examination revealed a 7 x 9mm raised, fleshy, whitish to pinkish, vascularized iris mass at the 2 o`clock position OD. Fundic examination showed multifocal round, brown to black, slightly raised lesions with indistinct margins and a surrounding hyperreflective zone OU. Physical examination revealed a temperature of 39.2°C, sinus tachycardia, preputial and ventral edema, and an enlarged right mandibular lymph node. Results of a complete blood count and plasma biochemical profile showed mild anemia, leukocytosis, and thrombocytopenia. Severe splenopathy, moderate splenomegaly and severe pulmonary pathology with nodules and large areas of consolidated lung parenchyma were observed on abdominal ultrasound and thoracic radiographs, respectively. Fine needle aspirates of the enlarged mandibular lymph node showed malignant epithelial neoplastic cells. The horse was euthanized because of the poor prognosis and subsequently underwent postmortem examination. Macroscopic necropsy and histopathology revealed an adenocarcinoma of suspected pulmonary origin with involvement of both eyes, heart, liver, kidneys, spleen, diaphragm, skeletal muscles, mandibular, pulmonary and internal iliac lymph nodes. Metastatic adenocarcinoma should be considered as a differential diagnosis in horses with iris masses, multifocal chorioretinal infiltrates, and clinical signs that conform to a paraneoplastic syndrome.

Key Words: eye, horse, neoplasia, adenocarcinoma, metastatic, paraneoplastic syndrome

CASE REPORT

A 10-year-old German Warmblood gelding was referred to the Equine Department of the Vetsuisse Faculty, University of Zurich, Switzerland for an iris mass OD that had been observed one week prior to presentation, intermittent fever for the last 10 days and lethargy and coughing since 3 weeks. A complete ophthalmic examination was performed with slit lamp biomicroscopy (Kowa SL-15; Kowa Company Ltd, Tokyo, Japan) and indirect ophthalmoscopy (Omega 500; Heine, Ettenheim, Germany). The examination of the right eye revealed a positive menace response and dazzle reflex, whereas the pupillary light response was negative due to prior administration of topical atropine by the referring veterinarian. The anterior chamber showed a 1+ flare (grading scale for flare from 0-4+: 1+= mild, 2+=moderate, 3+=marked, 4+=severe). A 7 x 9 mm raised, fleshy, whitish to pinkish, vascularized iris mass at the 2 o'clock position almost touching the corneal endothelium was noted (Fig. 1). Fundic examination showed multifocal round, brown to black, slightly raised lesions with indistinct margins and a surrounding hyperreflective zone (Fig. 2). The lesions were approximately one third to two times the size of the optic nerve head. The optic nerve head was unremarkable. Intraocular pressure (IOP) measured by rebound tonometry (Tonovet ®; Tiolat, Espoo, Finland) was 11mmHg in the right eye. The left eye did not show any abnormalities in the anterior segment, but almost identical fundic lesions as described for the right eye were observed and the IOP was 13mmHg.

Ophthalmic examination findings were consistent with mild anterior uveitis, an iris mass in the right eye and chorioretinal infiltrates in both eyes. Differential diagnosis for the iris mass was primary or secondary neoplasia. Based on the patient history and coexisting clinical symptoms, differentials for the anterior uveitis and chorioretinal infiltrates included systemic infectious diseases caused by viruses (EHV-1 and 2, equine influenza, equine viral arteritis, Parainfluenza type 3), bacteria (Leptospira spp., Brucella spp., Streptococcus spp.,

Rhodococcus equi, Borrelia burgdorferi), parasites (Onchocerca spp., Strongylus spp., Toxoplasma gondii), endotoxemia, septicemia or neoplasia.(1)

Physical examination revealed a rectal body temperature of 39.2°C, sinus tachycardia (64 bpm), preputial and ventral edema, an enlarged right mandibular lymph node and slightly forced vesicular lung sounds. The remainder of the physical examination was unremarkable. Complete blood count and biochemistry showed mild anemia, leukocytosis and thrombocytopenia. Abnormal blood parameters are summarized in table 1. Fine needle aspirates from the enlarged right mandibular lymph node were conducted and submitted for cytologic evaluation. Malignant epithelial neoplastic cells were observed in the cytology smears.

Ultrasonographic examination of the abdomen revealed severe splenopathy due to multiple well-defined hypoechoic nodules and moderate splenomegaly. Thoracic radiographs showed severe lung pathology with multiple small nodules and large areas of consolidated lung parenchyma caudodorsally suggestive for a neoplastic disease.

Due to the findings consistent with a disseminated epithelial neoplasia and resulting poor prognosis, the horse was euthanized and underwent postmortem examination.

Gross pathologic findings included multiple disseminated white nodules of various sizes (from 1mm up to 5 cm) in all internal organs, diaphragm, and skeletal muscles. The nodules were firm elastic and the neoplasm was bulging over the cut surface. Histopathology of the anterior segment of the uvea showed a mild diffuse infiltrate of mainly lymphocytes and plasma cells representing an anterior uveitis. A cell-rich, infiltrating epithelial mass affected and replaced almost the whole iris (Fig. 3) and larger parts of the ciliary body (Fig. 4 A) of the right eye. Multifocal, slightly raised (approximately 1.5 mm) masses were observed in the choroid (Fig. 5A) of both eyes. Metastases were found in nearly all smaller vessels of the choroid, ciliary body and even retina. The neoplastic cells formed small acini and tubular

structures or small solid nests, which were divided by a fine fibrovascular stroma. The neoplastic cells showed a small amount of eosinophilic cytoplasm with clear cell borders and round nuclei, up to 7μm in diameter, with a vesicular chromatin pattern and often one distinct nucleolus (Fig. 4B). The mitotic rate was up to 15 mitotic figures per 10 HPFs but atypical mitotic figures were rarely observed. Emboli of tumor cells were visible in numerous small veins (Fig. 5B). Due to these findings the diagnosis of a metastatic adenocarcinoma was made. The primary origin of the adenocarcinoma could not be definitely identified, though in some histological sections of the choroid and other organs the neoplastic cells formed occasional cilia that aroused the suspicion of a bronchial origin of the neoplasm (Fig. 6).

The chorioretinal lesions were most likely caused by hematogenous spread of neoplastic epithelial cells invading the choroidal vessels and small choroidal capillaries leading to retinal detachment and retinal degeneration surrounding and overlying the choroidal neoplastic infiltrates. The retinal detachment was characterized by a hyperplasia of the retinal pigment epithelium (tombstone formation). The degeneration consisted of loss of neurons and thinning of the inner plexiform layer.

Identical infiltrates were found in the heart, liver, kidneys, spleen, lungs, diaphragm, skeletal muscles, mandibular, pulmonary and internal iliac lymph nodes.

DISCUSSION

The most commonly reported ocular tumors in horses affect the adnexal structures of the eye. Squamous cell carcinoma is the most common tumor of the eye and adnexa in the horse.(2) Ocular tumors may be primary or secondary from metastastic disease or local invasion. Metastatic neoplasia from lymphoproliferative disorders (lymphosarcoma) is the most common systemic neoplasia affecting the equine eye and has been described to involve the ocular and/or periocular structures.(3-6) Multiple myeloma has been described to metastasize into the eye and induce uveitis, intraocular and scleral hemorrhage, retinal detachment, and

blindness in combination with signs of systemic illness.(4) There is one case report of metastasis of a thyroid carcinoma to the uveal tract of a horse with a therapy resistant uveitis.(7)

To the best of the author's knowledge, this is the first case report describing a metastatic adenocarcinoma in the anterior (right eye) and posterior uvea (both eyes) with widespread metastasis in every internal organ in a horse. In the cat, pulmonary adenocarcinoma with ocular involvement has been described.(8-12) Typical findings in these cases were wedge-shaped areas of chorioretinal degeneration, most prominent in the tapetal fundus due to thrombi or emboli to the chorioretinal arteries, infarction, and secondary tapetal and sensory retinal necrosis. Anterior uveitis (9-12) and an iridal mass (11) were also diagnosed. In the present case, fundic examination revealed multifocal round, brown to black, slightly raised lesions with indistinct margins and a surrounding hyperreflective zone in both eyes. Histopathology showed that the lesions were most likely caused by hematogenous spread of neoplastic epithelial cells invading the choroidal vessels and small choroidal capillaries leading to retinal degeneration surrounding and overlying the choroidal neoplastic infiltrates. The occurrence of metastatic lesions in the posterior segment of both eyes is probably the result of the rich blood supply to the posterior uvea. Anterior uveitis in the right eye was most likely due to the iridal mass with subsequent inflammation of the iris and infiltrative growing neoplastic cells in the ciliary body leading to a disruption of the blood-aqueous barrier. Abnormal findings in the physical examination like fever, reported to be intermittent since 10 days, ventral and preputial edema as well as abnormal findings in the blood work (anemia, leukocytosis, and thrombocytopenia) are clinical signs that can be part of a paraneoplastic syndrome. A paraneoplastic syndrome is defined as a disease or symptom that is a consequence of the presence of neoplasia, but is not due to the local presence of neoplastic cells.(13) Nonspecific intermittent or remittent fevers are the most commonly found

paraneoplastic syndrome, resulting from the excessive release of cytokines by the neoplastic cells. Anemia in cancer patients may occur as a result of chronic disease, autoimmune hemolytic, microangiopathic or aplastic anemia. Thrombocytopenia may have multiple causes in neoplastic disorders such as increased platelet consumption, sequestration in the spleen or a decreased production due to bone marrow involvement.(13)

The primary origin of the adenocarcinoma could not be definitely identified, though in some histological sections of the choroid and other organs ciliated neoplastic cells were occasionally seen. Because of the severe lung pathology, a primary pulmonary origin of this adenocarcinoma with widespread metastasis was therefore presumed.

Metastatic adenocarcinoma should be considered as a differential diagnosis in horses with iris masses, multifocal chorioretinal infiltrates, and clinical signs that conform to a paraneoplastic syndrome.

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Table 1: Abnormal findings of complete blood count and biochemistry.

Blood parameter	Measured	Normal range[1]
Hematocrit (%)	25	30-42
Total protein (g/l)	77	60-70
White Blood Count (*10^3/µl)	11,2	4,7-8,2
Platelet count (*10^3/µl)	70	119-250
Blood urea nitrogen (mmol/l)	9	3.5-7
Alkaline phosphatase (U/l)	186	81-183
Glutamate dehydrogenase (U/l)	3.8	0.5-2.2
Aspartate aminotransferase (U/l)	497	229-393
Bilirubin (µmol/l)	109.6	17.4-35.2
Lactate dehydrogenase (U/l)	9122	369-822
Sodium (mmol/l)	138	139-147
Chloride (mmol/l)	90	102-110
Magnesium (mmol/l)	0.47	0.6-0.8
Phosphate (mmol/l)	1.7	0.7-1.3

[1]5% and 95% percentile

Figure 1: Clinical photograph of the right eye, showing the iris mass at initial presentation.

Figure 2: Fundus photograph of the right eye showing multifocal round, brown to black, slightly raised lesions with indistinct margins and a surrounding hyperreflective zone in the tapetal fundus.

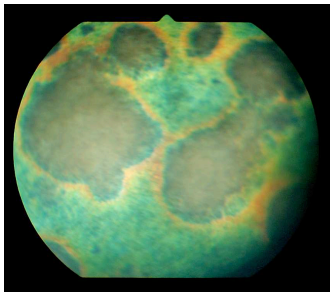
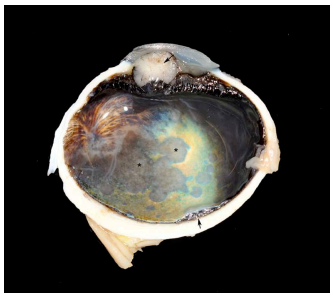


Figure 3: Hemisection of the right eye after formalin fixation showing the iris mass (arrow) and neoplastic chorioretinal infiltrates (asterisks) are easily identified. Neoplastic thickening of the choroid is obvious at the sectioned edge (arrowhead).



of the choroid is obvious at the sectioned edge (arrowhead).

Figure 4: Histological section (H&E) of the ciliary body. (A) Showing infiltrative growing epithelial neoplastic cells forming small acini and tubular structures (arrows) or small solid nests (asterisk), which are divided by a fine fibrovascular stroma (arrowheads). Scale bar = 200 µm. (B) Higher magnification showing the neoplastic cells having a small amount of eosinophilic cytoplasm and round nuclei, up to 7µm in diameter, with a vesicular chromatin pattern and often one distinct nucleolus. The mitotic rate is moderate. Scale bar = 50 µm.

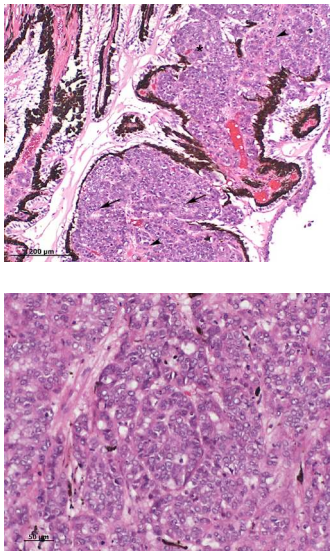


Figure 5: Histological section (H&E) of the choroid. (A) Emboli of neoplastic cells in medium-sized choroidal vessels (arrows) and neoplastic choroidal infiltrates (asterisk). Scale bar = 200 µm. (B) Embolus of neoplastic cells in a small choroidal capillary (arrow). Scale bar = 50 µm.

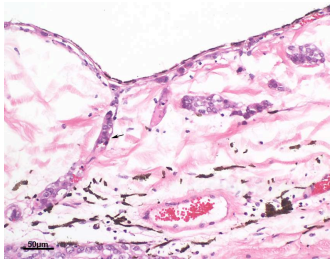


Figure 6: Histological section (H&E) of the choroid. Higher magnification of the neoplastic cells in the choroid. Some neoplastic cells show cilia (arrows) on the apical cell borders within a tubular lumen. Scale bar = 50µm.